

**Remarks**

This paper is submitted in response to the Office Action dated June 14, 2004. Applicants appreciate Examiner's decision that claims 38-41 and 43 are allowable. In response to the Office Action, claims 49-50, 52-54 and 60-61 have been canceled, claims 42, 51 and 55-59 have been amended, and claims 62-63 are new. Therefore, claims 31, 35, 42, 47, 48, 51, 55-59 and 62-63 are pending. Claims 31, 35 and 47-48 have been withdrawn from consideration by the Examiner.

Claims 42, 55-56 and 58 have been amended to depend from allowable claim 38 so that they encompass the tetragonal crystal of Hepatitis C virus helicase. Claim 51 has been amended to depend from allowable claim 38 so that it encompasses the tetragonal crystal of Hepatitis C virus helicase and amended to delete "wherein the crystal effectively diffracts x-rays to a resolution of 1.5 Å to 3 Å." Claims 57 and 59 have been amended to depend from allowable claim 40 so that they encompass the orthorhombic crystal of Hepatitis C virus helicase.

New claim 62 is supported by the specification at, for example, pages 30 and 42 (Table 4). New claim 63 is supported by the specification at, for example, page 29.

Applicants respectfully request that the Examiner reconsider and withdraw the rejections and enter, consider and allow the new claims.

**Objection to the Title**

The Examiner objects to the title because it includes reference to "methods," which are not among the elected claims. Applicants respectfully request that the Examiner hold this objection in abeyance until it is determined whether the method claims are allowable.

**Rejections under 35 U.S.C. §112, First Paragraph**

The Examiner rejected claims 42 and 49-61 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the claimed invention.

Claims 42, 55-56 and 58 have been amended to depend from allowable claim 38, thereby incorporating the enabled tetragonal crystal of Hepatitis C virus helicase. Claims 57 and 59 have been amended to depend from allowable claim 40, thereby incorporating the orthorhombic crystal of Hepatitis C virus helicase. Claim 51 has been amended to depend from allowable claim 38 so that it encompasses the tetragonal crystal of Hepatitis C virus helicase and amended to delete "wherein the crystal effectively diffracts x-rays to a resolution of 1.5 Å to 3 Å."

The Examiner asserts that Examples 4 and 5 (pages 49-50), which describe the preparation of a helicase/ligand complex for tetragonal and orthorhombic forms of Hepatitis C virus helicase crystals, respectively, are not enabling for the formation of co-crystals because providing generic guidelines would require a skilled artisan to engage in undue experimentation. Applicants respectfully disagree. A skilled artisan will understand that the provided methods support formation of helicase/ligand complexes independent of the particular characteristics of the chemical entity. Rather, to form these complexes, it is crucial to ascertain conditions suitable for complex formation for the

particular crystal type. This is exemplified by Examples 4 and 5 because different conditions for co-crystal formation were required for the tetragonal and orthorhombic crystal forms of Hepatitis C virus helicase. Examples 4 and 5 provide complex formation methodologies for the tetragonal and orthorhombic forms of Hepatitis C virus helicase crystals, respectively. Although some experimentation may be required to form co-crystals, such experimentation would not be undue because the specification provides reasonable parameters that enable a skilled artisan to form a co-crystal. Additionally, applicants are not required to submit every detail for the purposes of enablement. "Chemical entities" is sufficiently defined on page 18 as follows: "A "chemical entity," as that term is used herein, includes chemical compounds, complexes of two or more chemical compounds, and fragments of such compounds or complexes."

Furthermore, a skilled artisan will recognize that the unit cell dimension and space group characteristics of the crystal will change only very slightly, if at all, upon introduction of a chemical entity post-formation of the crystal. Therefore, since the particularly claimed tetragonal and orthorhombic crystals of Hepatitis C virus helicase are enabled, providing methods for forming co-crystals for the particular crystal forms enables the co-crystals.

Applicants respectfully point out that no specific claims are made encompassing co-crystals. Rather, withdrawn claims 47 and 48 claim methods for incorporating chemical entities into each of the two allowable crystal structures for Hepatitis C virus helicase. These methods are well-supported in Examples 4 and 5. Thus, applicants believe that upon rejoinder, claims 47-48 are in condition for allowance.

Claims 49-50, 52-54 and 60-61 are canceled and we reserve the right to pursue the subject matter of these claims in any future continuing or divisional applications.

Claims 42 and 49-61 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the invention was filed, had possession of the claimed invention.

The Examiner rejects claims 42 and 49-61 for failure to recite the particular unit cell dimensions that are supported in the application, which the Examiner asserts causes the claims to cover crystals other than those enabled and supported in the specification. The Examiner further rejects claims 42 and 50-51 for applying open claim language ("having" and "comprising") to SEQ ID NO:1, which the Examiner asserts results in unsupported genus claims. As detailed below, to advance the application towards allowance, currently pending claims have been amended to cite the particular unit cell dimensions supported in the application and the claim language pertaining to SEQ ID NO:1 has been amended.

Claims 42, 51, 55-56 and 58 have been amended to depend from allowable claim 38, thereby incorporating the enabled tetragonal crystal of Hepatitis C virus helicase. Claims 57 and 59 have been amended to depend from allowable claim 40, thereby incorporating the orthorhombic crystal of Hepatitis C virus helicase.

Applicants respectfully disagree with the Examiner's assertion that the open language "having" and "comprises" as found in claims 42 and 51, respectively, with regard to SEQ ID NO:1 establishes

these claims as unsupported genus claims. One of skill in the art would recognize that in this instance "having" and "comprising" invoke minor variations of SEQ ID NO:1. Such variants would still require that they result in crystals with the described unit cell dimensions. However, in the interest of advancing the claims to allowance, claims 42 and 51 have been amended as indicated herein.

**New Claims**

New claim 62 recites the Hepatitis C virus helicase crystal with unit cell dimensions of allowable claim 40 with the added provision that the crystal diffracts x-rays to a resolution of 1.5 Å to 3 Å, which is supported in the specification on pages 30 and 42 (Table 4).

New claim 63 recites Hepatitis C virus helicase crystal with unit cell dimensions of allowable claim 40 with the added provision that the Hepatitis C virus peptide has at least one cysteine or methionine replaced by selenocysteine or selenomethionine, respectively. This is supported in the specification on page 29.

Applicants respectfully request that the Examiner enter, consider and allow new claims 62-63.

**Request for Rejoinder**

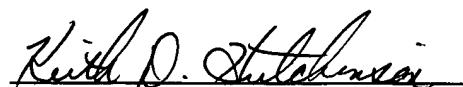
As indicated by the Examiner, rejoinder for method claims 31, 35 and 47-48 will occur upon allowance of the product claims. Applicants respectfully assert that because product claims 58-59 are now allowable and because claims 38-41 and 43 were previously determined to be allowable, the method claims 31, 35 and 47-48 are suitable for rejoinder.

**Summary**

In view of the foregoing claim cancellations and amendments, Applicants believe all of the stated grounds of the rejections have been properly traversed and overcome. Therefore, Applicants respectfully request that the outstanding rejections be withdrawn and claims 31, 35, 42, 47-48, 51, 55-59 and 62-63 be allowed. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

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